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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/720,788	11/24/2003	Roger Edward Markwell	P32371-C1	4626

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EXAMINER	
SEAMAN, D MARGARET M	
ART UNIT	PAPER NUMBER
1625	

DATE MAILED: 09/01/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/720,788	MARKWELL ET AL.	
	Examiner	Art Unit	
	D. Margaret Seaman	1625	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-11 and 13* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☒ Claim(s) *9* is/are allowed.

6)☒ Claim(s) *1-8,10,11 and 13* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

This application was filed 24 November 2003 and is a CON of 10/031,768 (Filed 7/17/2002 ABN) which is a 371 of PCT/EP00/06940 (7/17/2000). Claims 1-11 and 13 are before the Examiner.

Claim Rejections - 35 USC § 112

1. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

2. Claims 1-8, 10, 11 and 13 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for compounds having a quinoline core (i.e. Z1-Z5 being other than CH or one being CR1a when R1a is hydrogen), R1 as methoxy and R5 being alkyl, does not reasonably provide enablement for R1 being alkoxy substituted by piperidyl, guanidine or other substitutients other than methoxy; R5 being hydroxycycloalkyl, cyano, substituted phenyl alkyl, or substituted benzoyl among others. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make the invention commensurate in scope with these claims. The specification and claims have many substitutients listed including natural amino acid side chains or their enantiomers but

only makes and enables the substitutients wherein R1 is methoxy, Z1-Z5 being CH or CR1a wherein R1a is hydrogen, and R5 being other than alkyl.

There are many factors to be considered when determining whether there is sufficient evidence to support a determination that a disclosure does not satisfy the enablement requirement and whether any necessary experimentation is "undue". These factors include 1) the breadth of the claims, 2) the nature of the invention, 3) the state of the prior art, 4) the level of one of ordinary skill, 5) the level of predictability in the art, 6) the amount of direction provided by the inventor, 7) the existence of working examples, and 8) the quantity of experimentation needed to make or use the invention based on the content of the disclosure. In re Wands, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988).

The nature of the invention: The nature of the invention is the method of treating a bacterial infection using a compound of claim 1 (claim 11).

The state of the prior art: The state of the prior art is that it involves screening in vitro and in vivo to determine which compounds exhibit the desired pharmacological activities (i.e. what compounds can treat which specific disease). There is no absolute predictability even in view of the seemingly high level of skill in the art. The existence of these obstacles establishes that the contemporary knowledge in the art would prevent one of ordinary skill in the art from accepting any therapeutic regimen on its face.

The predictability in the art: It is noted that the pharmaceutical art is unpredictable, requiring each embodiment to be individually assessed for physiological activity. In re Fisher, 427 F. 2d 833, 166 USPQ 18 (CCPA 1970) indicates that the more unpredictable an area is, the more specific enablement is necessary in order to satisfy the statute. In the absence of a showing of a nexus between all of the instantly claimed substitutients and the actual made and tested substitutients of R1 is methoxy, Z1-Z5 being CH or CR1a wherein R1a is hydrogen, and R5 being other than alkyl and the treatment of all bacterial infections, one of ordinary skill in the art is unable to fully predict possible results from the administration of the compound of claim 1 outside of the scope outlined above, due to the unpredictability of the role of bacterial infections.

The presence or absence of working examples: The compounds of examples 1-7 contain only a very small amount of substitution from a very broad group of substitutients available in claim 1. It is known in other quinoline antibacterial compounds that the presence of a 6-position fluorine radically changes the activity from a 6-position chlorine substitutient. Since this is known in the art, how can a showing of a substitutient being methoxy working as an antibacterial equating the substitutients of alkylsulphonyloxy, guanidino optionally substituted by alkylsulphonyl or CH(natural amino acid side chain enantiomer)COOH.

The amount of direction or guidance present: The guidance present in the specification is that all of the compounds within the scope of claim 1 work. However, there is no actual guidance to choose a subsitutient other than those very few that are

exemplified by the seven examples given in the specification that have R1 is methoxy, Z1-Z5 being CH or CR1a wherein R1a is hydrogen, and R5 being alkyl.

The breadth of the claims: The claims are drawn to the treatment of bacterial infections with the compounds of claim 1.

The quantity of experimentation needed: The quantity of experimentation needed is undue to enable the entire scope of claim 1. One skilled in the art would need to determine what substitutients out of all of the substitutients available would benefit the treatment of bacterial infections.

The level of the skill in the art: The level of skill in the art is high. However, due to the unpredictability in the pharmaceutical art, it is noted that each embodiment of the invention is required to be individually assessed for physiological activity by in vitro and in vivo screening to determine which compounds exhibit the desired pharmacological activity and which diseases would benefit from this activity.

Thus, the specification fails to provide sufficient support of the use of the full scope of the compounds within claim 1 for the treatment of bacterial infections. As a result necessitating one of ordinary skill to perform an exhaustive search for which diseases can be treated by which compound of claim 1 in order to practice the claimed invention.

Genentech Inc. v. Novo Nordisk A/S (CA FC) 42 USPQ2d 1001, states that "a patent is not a hunting license. It is not a reward for search, but compensation for its

successful conclusion" and "[p]atent protection is granted in return for an enabling disclosure of an invention, not for vague intimations of general ideas that may or may not be workable".

Therefore, in view of the Wands factors and In re Fisher (CCPA 1970) discussed above, to practice the claimed invention herein, one of ordinary skill in the art would have to engage in undue experimentation to test which substitutients on the main core outside of the small scope disclosed by the specification can be used to treat bacterial infections, with no assurance of success.

This rejection can be overcome by deleting the scope of the claims outside of R1 is methoxy, Z1-Z5 being CH or CR1a wherein R1a is hydrogen, and R5 being alkyl.

3. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

4. Claim 2 recites the limitation "Z3 may be CF". There is insufficient antecedent basis for this limitation in the claim. Claim 1 (from which claim 2 depends) does not have Z3 being CF. Correction is required.

Allowable Subject Matter

5. Claim 9 is allowable over the prior art of record. The closest art is Myers that teaches similar quinoline compounds. However, the compounds of Myers do not anticipate or make obvious the instant claim 9.

6. Any inquiry concerning this communication or earlier communications from the examiner should be directed to D. Margaret Seaman whose telephone number is 571-272-0694. The examiner can normally be reached on 630am-4pm, First Friday Off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Cecelia Tsang can be reached on 571-272-0562. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

D. Margaret Seaman
Primary Examiner
Art Unit 1625

dms